

ATATTGCTGAGCTCAGGGAGTGAGGGCCCCACATTTGAGACAGTGAGCCCCAAGAAGAG	60
GATCCCTGCTCCAGCAGCTGCAAGGTGCAAGAAGAAGAAGATCCCAGGGAGGAAAATGTG	120
CTGGAGACCCCTGTGGGTTCCTGTGGTCTTATCTTCTATGTTCAAGCAGT	180 22
GCCTATCCAGAAAGTCCAGGATGACAGCCAAAACCCTCATCAAGACCATTGTCACCAGGAT P 1 Q K V Q D D $\tau$ K $\tau$ L I K $\tau$ 1 V $\tau$ R I	240 42
CAATGACATTTCACACACGCAGTCGGTTATCCGCCAAGCAGAGGGGTCACTGGCTTTGGACTT N D I S H T O S V S A K Q R V T G L D F	300 62
CATTCCTGGGCTTCACCCCATTCTGAGTTTGTCCAAGATGGACCAGACTCTGGCAGTCTA	360 82
TCAACAGGTCCTCACCAGCCTGCCTTCCCAAAATGTGCTGCAGATAGCCAATGACCTGGA Q Q V L T S L P S Q N V L Q I A N D L E	420 102
GAATCTCCGAGACCTCCTCCATCTGCTGGCCTTCTCCAAGAGCTGCTCCCTGCCTCAGAC N L $\frac{R}{L}$ D L L H L L A F S K S C S L P Q T	480 122
CAGTGGCCTGCAGAAGCCAGAGAGCCTGGATGGGGTCCTGGAAGCCTCACTCA	540 142
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	600 162
TGTTAGCCCTGAATGCTGAAGTTTCAAAGGCCACCAGGCTCCCAAGAATCATGTAGAGGG V 3 P E C	660 167
AAGAAACCTTGGCTTCCAGGGGTCTTCAGGAGAAGAGACCATGTGCACACATCCATC	720
TCATTTCTCTCCCTCTGTAGACCACCCATCCAAAGGCATGACTCCACAATGCTTGACTC	780
AAGTTATCCACACACTTCATGAGCACAAGGAGGGGGCCAGCCTGCAGAGGGGACTCTCAC	840
CTAGTTCTTCAGCAAGTAGAGATAAGAGCCATCCCATCC	900
${\tt GGGTACATGTTCCTCCGTGGGTACACGCTTCGCTGCGGCCCAGGAGAGGTGAGGTAGGGA}$	960
TGGGTAGAGCCTTTGGGCTGTCTCAGAGTCTTTGGGAGCACCGTGAAGGCTGCATCCACA	1020
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TAATTTTTGAGTGACTGGAAGGAAGGTTGGGATCTTCCAAACAAGAGTCTATGCAGGTAG	1260
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ACGTTTGCAGCGGCATTGCCGGGAGCATAGGCTAGGTTATTATCAAAAGCAGATGAATTT	1380
TGTCAAGTGTAATATGTATCTATGTGCACCTGAGGGTAGAGGATGTGTTAGAGGGAGG	1440
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ACCCTACTCGCGGCGGTGTACTCCACCACAGCAGCACCGCACCGCTGGAAGTACAGTGCT	2220
GTCTTCAACAGGTGTGAAAGAACCTGAGCTGAGGGTGACAGTGCCCAGGGGAACCCTGCT	.2280
TGCAGTCTATTGCATTTACATACCGCATTTCAGGGCACATTAGCATCCACTCCTATGGTA	2340
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GGACTAGAAGAGTTTTGGATTTTAGAGTCTTTTCAGGCATAGGTATATTTTGAGTATATAT	2460
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GGGTTTTGGAGCAGTTTGGATCTTGGGTTTTCTGTTAAGAGATGGTTAGCTTATACCTAA	2700
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TCCAGCCAGGTCATACCCTGTGGAGGTGAGCGGGATCAGGTTTTGTGGTGCTAAGAGAGG	2820
AGTTGGAGGTAGATTTTGGAGGATCTGAGGGC	
un i innum i vi i i i i i i i i i i i i i i i i i	2852

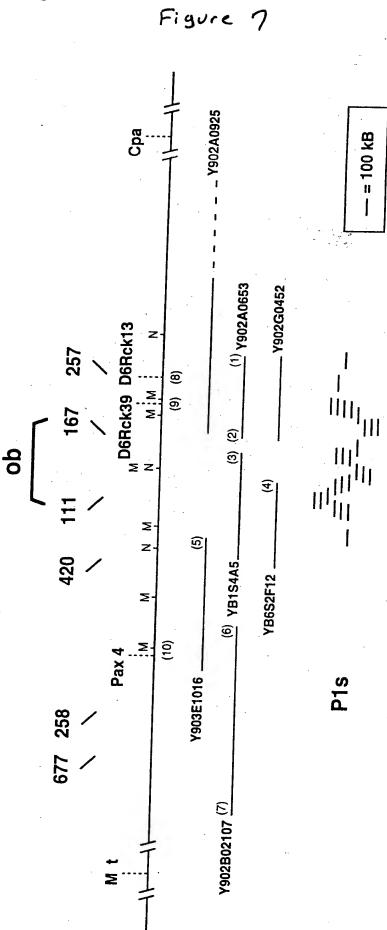
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TTGGGGAACC CTGTG-CGGA TTCTTGTGGC TTTGGCCCTA TCTTTTCTAT	100
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CAAGACAATT GTCACCAGGA TCAATCACAT TTTCACAT TTTCACAT	200
CCTCCAAACA GAAAGTCACC GGTTTGGACT TCATTCCTGG GCTCCACCCC	250
ATCCTGACCT TATCCAAGAT GGACCAGACA CTGGCAGTCT ACCAACAGAT	300
CCTCACCAGT ATGCCTTCCA GAAACGTGAT CCAAATATCC AACGACCTGG	350
AGAACCTCCG GGATCTTCTT CACGTGCTGG CCTTCTCTAA GAGCTGCCAC	400
TTGCCCTGGG CCAGTGGCCT GGAGACCTTG GACAGCCTGG GGGGTGTCCT	450
GGAAGCTTCA GGCTACTCCA CAGAGGTGGT GGCCCTGAGC AGGCTGCAGG	500
GGTCTCTGCA GGACATGCTG TGGCAGCTGG ACCTCAGCCC TGGGTGCTGA	550
GGCCTTGAAG GTCACTCTTC CTGCAAGGAC T-ACGTTAAG GGAAGGAACT	600
TTGGTTTCCA GGTATCTCCA GGATTGAAGA CCATTTGAAGA	
ATCCAGGACT CTGTCAATTT CCCTGACTCC TCTAAGGGAG	650
;	700
	701

1	Met	His	Trp	Gly	Thr	Leu	Cys	Gly	Phe	Leu	Trp	Leu	Trp	Pro	Tyr
16	Leu	Phe	Tyr	Val	Gln	Ala	Val	Pro	Ile	Gln	Lys	Val	Gln	Asp	Asp
31	Thr	Lys	Thr	Leu	Ile	Lys	Thr	Ile	Va1	Thr	Arg	Ile	Asn	Asp	Íle
46	Ser	His	Thr	Gln	Ser	Val	Ser	Ser	Lys	Gln	Lys	Val	Thr	Gly	Leu
61	Asp	Phe	Ile	Pro	Gly	Leu	His	Pro	Ile	Leu	Thr	Leu	Ser	Lys	Met
76	Asp	Gln	Thr	Leu	Ala	Val	Tyr	Gln	Gln	Ile	Leu	Thr	Ser	Met	Pro
91	Ser	Arg	Asn	Val	Ile	Gln	Ile	Ser	Asn	Asp	Leu	Glu	Asn	Leu	Arg
L06	Asp	Leu	Leu	His	Val	Leu	Ala	Phe	Ser	Lys	Ser	Cys	His	Leu	Pro
.21	Trp	Ala	Ser	Gly	Leu	Glu	Thr	Leu	Asp	Ser	Leu	Gly	Gly	Val	Leu
.36	Glu	Ala	Ser	Gly	Tyr	Ser	Thr	Glu	Val	Val	Ala	Leu	Ser	Arg	Leu
51	Gln	Gly	Ser	Leu	Gln	Asp	Met	Leu	Trp	Gln	Leu	Asp	Leu	Ser	Pro
66	Gly	Cys	End				•								٤

Mouse	MCWRPLCRFL	WLWSYLSYVQ	AVPIQKVQDD	TKTLIKTIVT	RINDISHTQS	50
Human	MHWGTLCGFL	WLWPYLFYVQ	AVPIQKVQDD	TKTLIKTIVT	RINDISHTQS	
Mouse	VSAKQRVTGL	DFÍPGLHPIL	SLSKMDQTLA	VYQQVLTSLP	SONVLQIAND	100
Human	VSSKOKVTGL	DFIPGLHPIL	TLSKMDQTLA	VYQQILTSMP	SRNVIQISND	
Mouse	LENLRDLLHL	LAFSKSCSLP	QTSGLQKPES	LDGVLEASLY	STEVVALSRL	150
Human	LENLRDLLHV	LAFSKSCHLP	WASGLETLDS	LGGVLEASGY	STEVVALSRL	
Mouse	QGSLQDILQQ	LDVSPEC				167
Human	OGSTODMENO	LDLSPGC			•	

1	Me	t Cy	s Tr	Arg	Pro	Leu	Cys	Arg	y Pho	a Lei	ı Tre	Leu	Tre	Ser	- Tv+
16	Let	ı Ser	Tyr	Val	Gln	Ala	Va]	Pro	o Ile	a Gln	T.ve	V=7	G12	3.0-	
31	Thr	Lys	Thr	Leu	Ile	Lva	Thr	Tle	Val	The	. 273	**************************************	9111	ASC	ASP
46	Ser	His	Thr	Ser	Val	Ser	λ1 <i>a</i>	Tare				110	Aen	Asp -	Ile
61	Phe	Ile	Pro	Giv	T. 411	u i a	D	-1	- GIII	Arg	val	THE	GIĀ	Leu	Asp
76	Gln	Thr	Lou	Gly	77-7	ura	PIO	TTe	Leu	Ser	Leu	Ser	Lys	Met	Asp
91	G1-			Ala	Val	TYT	Gln	Gln	Val	Leu	Thr	Ser	Leu	Pro	Ser
1.7	GIN	Asn	Val	Leu	Gln	Ile	Ala	Asn	Asp	Leu	Glu	Asn	Leu	Arg	Asp
106	Leu	Leu	His	Lau	Leu	Ala	Phe	Ser	Lys	Ser	Суз	Ser	Leu	Pro	Gln
131	Thr	Ser	Gly	Leu	Gln	Lys	Pro	Glu	Ser	Leu	qzA	Glv	Val	Len	di.
136	Ala	Ser	Leu	Tyr	Ser	Thr	Glu	Val	Val	Ala	Len	Se-	3-0	<b>.</b>	
51	G1y	Ser	Leu	Gln i	Asp :	Ile :	Leu	Gln	Gln	Lou	A 1		nty .	ran	Gin
66	Cys	End								~~u .	web .	val :	ser :	Pro	Ġīn

Met His Trp Gly Thr Leu Cys Gly Phe Leu Trp Leu Trp Pro Tyr Leu Phe Tyr Val Gln Ala Val Pro Ile Gln Lys Val Gln Asp Asp Thr Lys Thr Leu Ile Lys Thr Ile Val Thr Arg Ile Asn Asp Ile Ser His Thr Ser Val Ser Ser Lys Gln Lys Val Thr Cly Leu Asp Phe Ile Pro Gly Leu His Pro Ile Leu Thr Leu Ser Lys Met Asp Gln Thr Leu Ala Val Tyr Gln Gln Ile Leu Thr Ser Met Pro Ser 76 Arg Asn Val Ile Gln Ile Ser Asn Asp Leu Glu Asn Leu Arg Asp Leu Leu His Val Leu Ala Phe Ser Lys Ser Cys Ris Leu Pro Trp 106 121 Ala Ser Gly Leu Glu Thr Leu Asp Ser Leu Gly Cly Val Leu Glu Ala Ser Gly Tyr Ser Thr Glu Val Val Ala Leu Ser Arg Leu Gln 136 Gly Ser Leu Gln Asp Met Leu Trp Gln Leu Asp Leu Ser Pro Gly 166 Cys End



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a)

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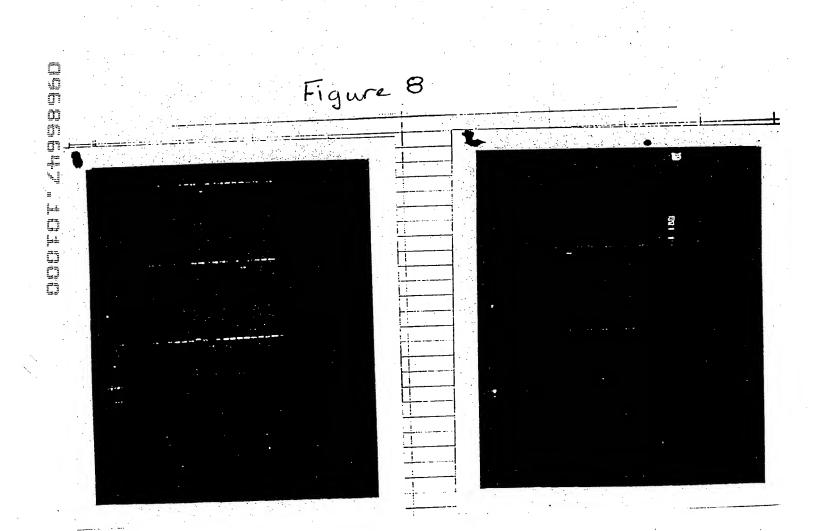


Figure 9

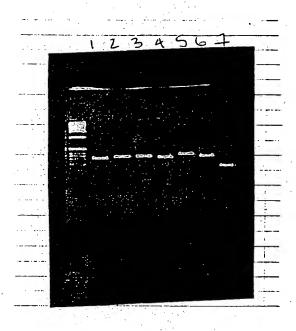
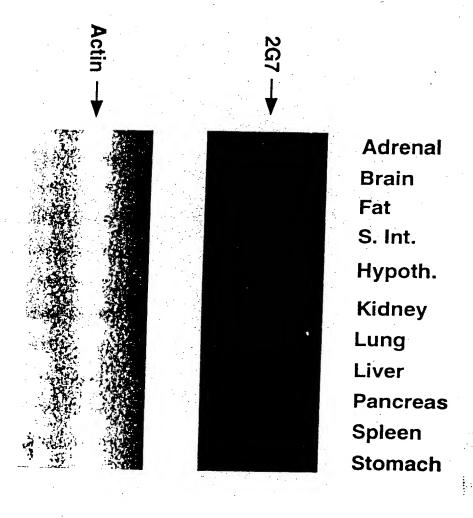


Figure 11A



#### Figure 11B

18S 1

white fat brain

small intestine

stomach

pancreas

lung

testis

heart

spleen

liver

Figure 12 B

brain SM/Ckc-+*Dac*-+/+ fat SM/Ckc-+*Dac-ob<sup>2J</sup>/ob<sup>2J</sup> fa* C57BL/6J +/+ fat C57BL/6J ob/ob fat

2G7

- 285

**- 18**S

Actin

- 185

Figure 12A

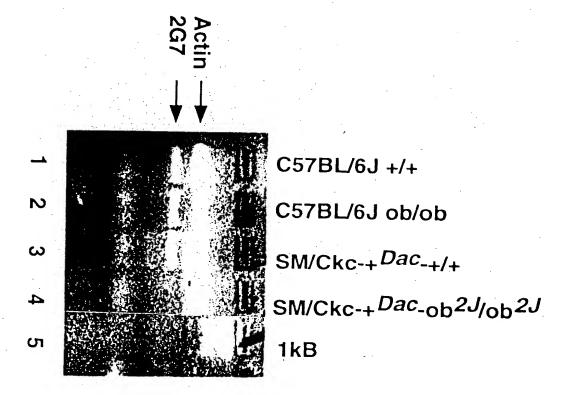
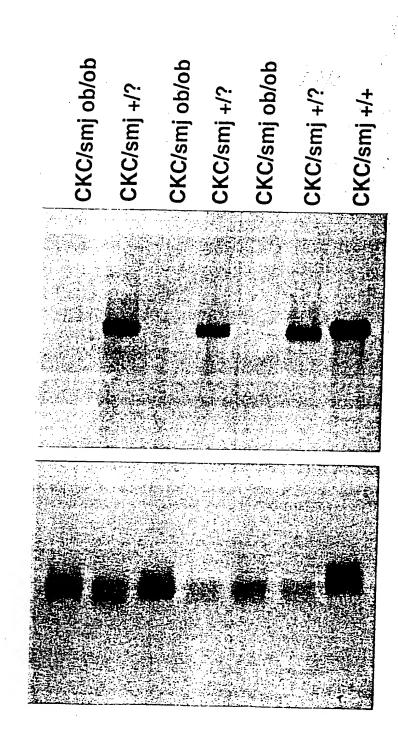


Figure 13

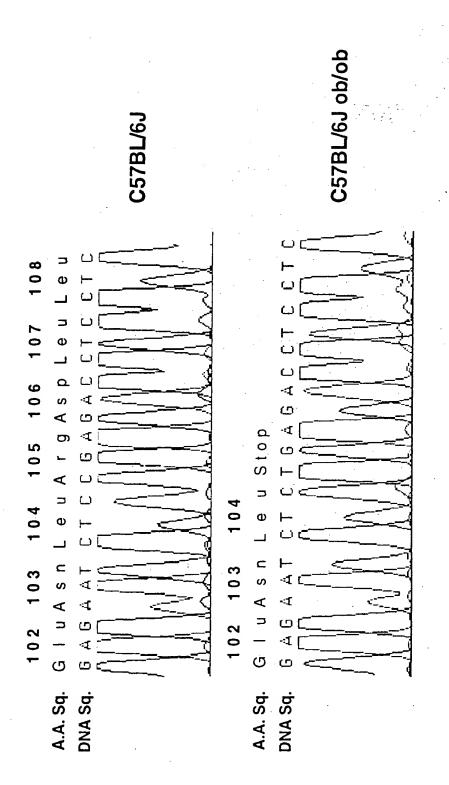


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2G7

ap2

Figure



#### Figure 15A

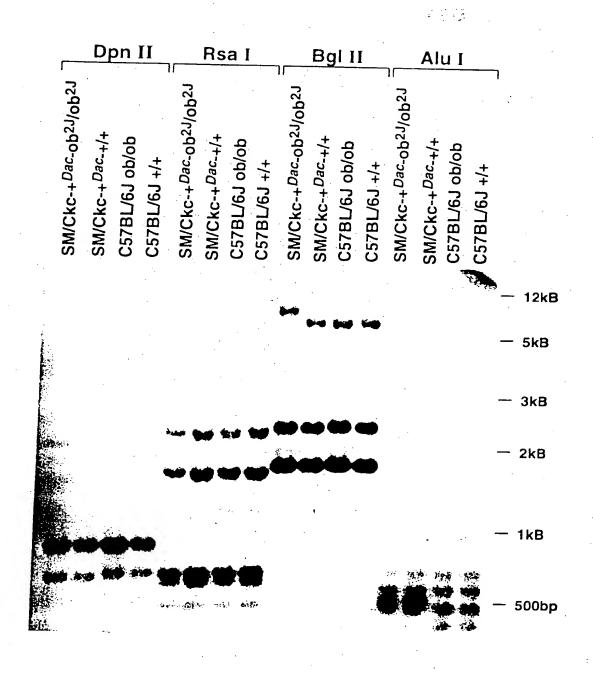
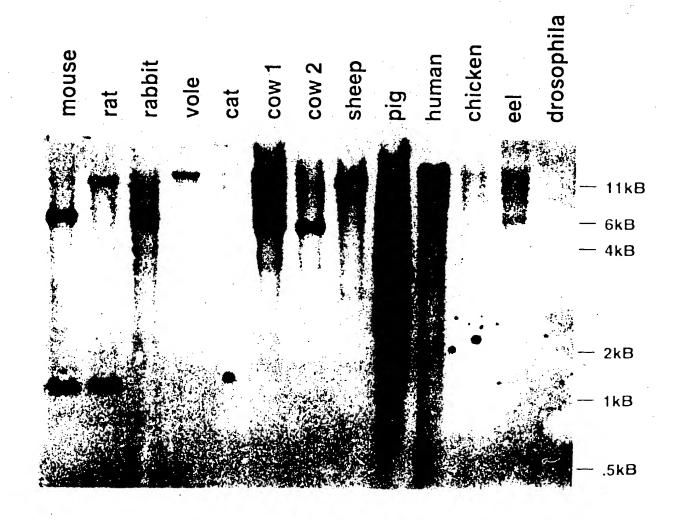


Figure 15B

obese stand obese stand obese lean obese see see see see see see obese obese obese obese obese obese

Figure 16



T7 promoter primer #69348-1

T7 lerminator primer #89337-1

Figure 18 A

Soluble
in soluble
Thou Thr.
5 mm

20 mm

20 mm

300 mm

stripping

41-= 31 - -=

4.3 -

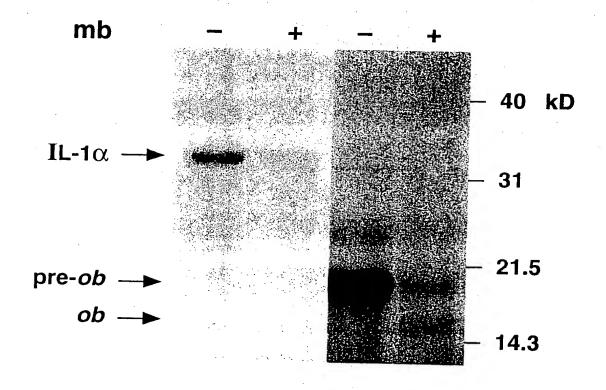
Figure 18B

Soluble
insoluble
Thur thr.
5 mm
20 mm
300 mm
300 mm

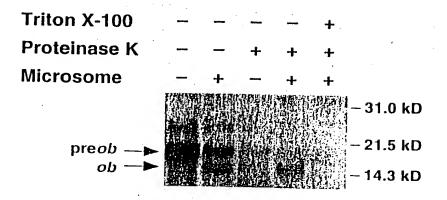
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L.

Figure 19A



### Figure 19B



### Figure 20A

	10	2	0 I	30	10 50 L I
	GGTTGCAAGG	CCCAAGAAG	C CCATCCTGG	G AAGGAAAAT	G CATTGGGGAA
	60	HOBLE 7	٥	30 ° 5	ြ <sup>စ်</sup> -100
	CCCTGTGCGG	ATTCTTGTG	G CTTTGGCCC	T ATCTTTTCT	A TGTCCAAGCT
	110		_	] -	10 150
	GTGCCCATCC	AAAAAGTCC	A AGATGACAC	C AAAACCCTC	A TCAAGACAAT
	160	17	0 1	40 <b>34</b> 2,04 1	1st NTRON
	TGTCACCAGG	ATCAATGAC	TTTCACACA	C GSTAAGGAG	A GTATGCGGG
	210	22	0 23	30 2	40 250
	ACAAAGTAGA	ACTGCAGCCA	GCCCAGCAC	T GGCTCCTAG	T GGCACTGGAC
	260	27	0 26	0 29	0 WOB 19 8300
1	CCAGATAGTC	CAAGAAACAT	TTATTGAAC	CCTCCTGAA	F GCCAGGCACC
	310	32	o 33	0 34	350
٦	TACTGCAAGC	TGAGAAGGAT	TTTGGATAGO	ACAGGGCTC	CACTCTTTCTG
	360	370			
1	GTTGTTTCTT 1	NTGCCCCCT	CTGCCTGCTG	AGATNCCAG	GGTTAGNGGT
	410	420	43	0 44	0 450
1	TCTTAATTCC :	TAAAA	46 065500	ENCE (2 1.	
1	460	470			0 500
1	GGTTCTTTCA (	GAAGAGGCC	ATGTAAGAGA	AAGGAATTGA	CCTAGGGAAA
	510	520			
7	ATTGGCCTGG G	AAGTGGAGG	GAACGGATGG	TGTGGGAAAA	GCAGGAATCT
ı	560	570			•
1	GGAGACCAG C	TTAGAGGCT	TGGCAGTCAC	CTGGGTGCAG	GANACAAGGG
1	670	620	630		
10	CTGAGCCAA A	GTGGTGAGG	GAGGGTGGAA	GGAGACAGCC	CAGAGAATGA
l	နေဝ	670	680		
7	CCTCCATGC C	CACGGGGAA	GGCAGAGGGC	TCTGAGAGCG	ATTCCTCCCA
	710	720	3. of 12 1	OTRON.	
10	ATGCTGAGC A	CTTGTTCTC	CCTCTTCCTC	CTNCATAGCA	GTCAGTCTCC
	HOB 28 - 760	770	780	•	800
T	CCAAACAGA A	AGTCACCGG	TTTGGACTTC	ATTCCTGGGC	TCCACCCCAT
	810	820	830	840	
Īē	CTGACCTTA TO	CCAAGATGG	ACCAGACACT	GGCAGTCTAC	CAACAGATCC
	860	870	890	8 90	900
T	CACCAGTAT GO	CTTCCAGA	AACGTGATCC	AAATATCCAA	CCACCTCCAC

	910	920	930	940	950
AACCTCC	GGG A1	CTTCTTCA CGT	GCTGGCC TTC:	CTAAGA GCT	GCCACTT
	960	970	980	990	1000
SCCCIGGO	GCC AC	TCGCCTGG AGAC	CCTTGGA CAG	CTGGGG GGT	STCCTGG
	1010	10,20	1030	10,40	1050
LAGCTTCA	IGG CT	ACTCCACA GAGO	TGGTGG CCCT	GAGCAG GCT	CAGGG
	1060	10,70	1080	1090	1100
CTCTGCA	GG AC	ATGCTGTG GCAG	CTGGAC CTCA	GCCCTG GGTG	CTGAGG
	1110	1120	1130	1140	1150
CTTGAAG	GT CA	CTCTTCCT GCAA	GGACTA CGTT	AAGGGA AGGA	ACTOTO
1	160	1170	1180	11,50	1200
CTTCCAG	GT AT	CTCCAGGA TTGA	AGAGCA TTGC	ATGGAC ACCC	CTTATC
	210	4092g1220	1230	12.40	1250

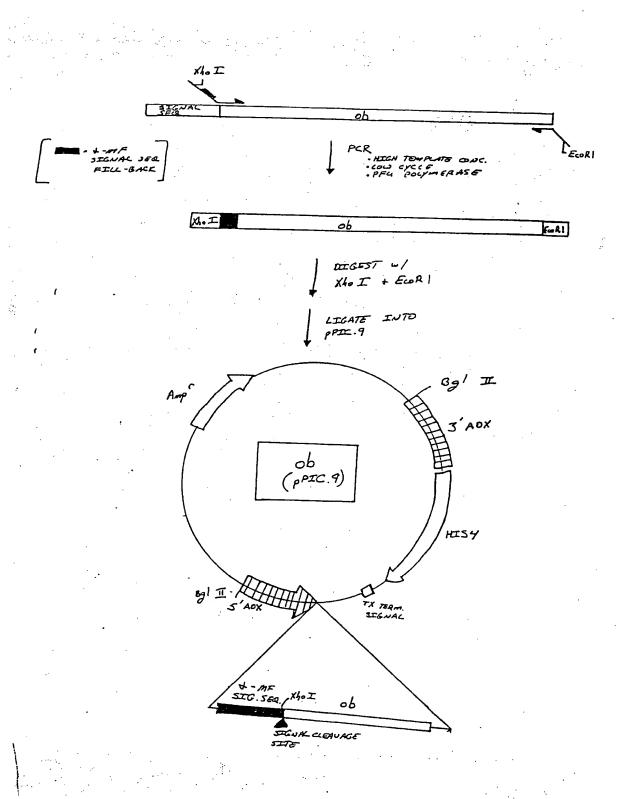
### Figure 20B

			•	·		
MOUS	SE OB ST	RUCIURE	3			
!st ex	!st intr		2nd intr	3rd exon	<b></b>	,
		start			TGA stop	
						•

### Figure 20c

HOMAIN OB	210	CIURE	•			
	lst	exon	1st intr	2nd exon		
***************************************	A7	rG			TGA	
	*	start			stop	

figure 21A



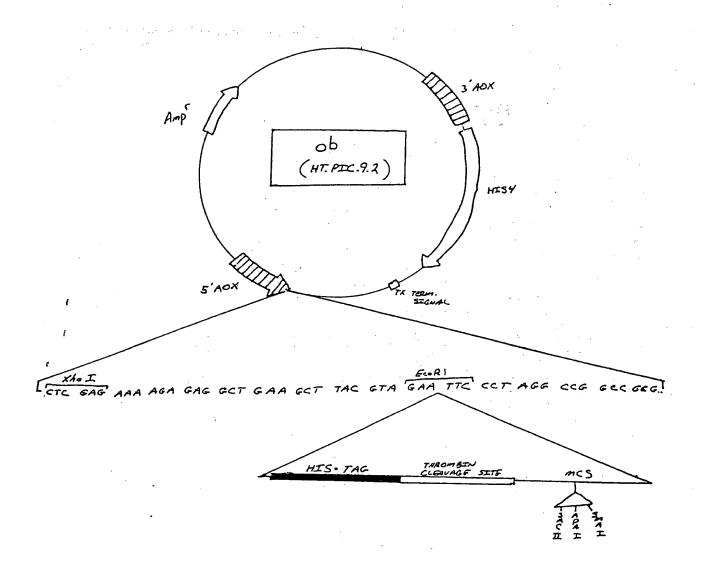
## Figure 21 B

VVV LE	1. GLU . LYS	· ARG · GLU · ALA · G	LU · ACA ·	ob	<u> </u>
• .				•	
		KEX-2	STE-13 CLEAVAGE		
		CLEAVAGE	?		
	*.	•	•	·	
		GLU·ACA·G	cu · ACA ·	ob	
	(X)		**• <b>•</b>		
		•	•	øb .	

Figure 21c

X4. I LEU. GLU. LY S. ARG.		
// / / / / / / / / / / / / / / / / / /	ob	
KEX - 2 CLEHUAGE	1	
·		٠.
	ob	

Figure 22A



100-1-087 CIP ( eet 30 of 31)

Figure 22B

d-MF SIG SEQ.	aco-sta	HIS.TAG	THEOMBEN CLO	PUACE		ob
	CLENVAGE	igvace			1	(FOLIOSING THROMBIN CLEAVAGE)
·			GLY · SER · PS	20.		٥b

Figure 23A.

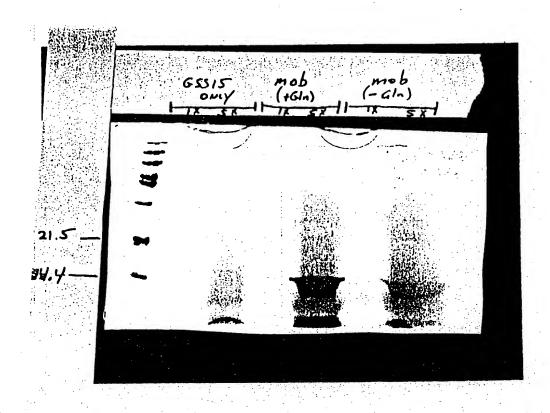


Figure 23B

